This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

E1

1. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal, said method comprising delivering to said tumor ~~administering to said mammal~~ a serum-stable nucleic acid-lipid particle comprising a nucleic acid portion that is fully encapsulated within the lipid portion,

wherein said delivering ~~administration~~ is by injection at an injection site that is distal to said tumor ~~neoplasia~~ in said mammal;

and wherein said lipid portion of said nucleic-acid lipid particle comprises a cationic lipid, a neutral lipid, and a lipid conjugate that prevents aggregation during formulation.

2. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 1, wherein said nucleic acid comprises an expressible gene.

3. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 2, wherein said expressible gene encodes a member selected from the group consisting of therapeutic polypeptides and therapeutic polynucleotides.

4. (Twice amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 2, wherein said gene is heterologous.

5. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 3, wherein said gene is a member selected from the group consisting of genes encoding suicide enzymes, toxins and ribozymes.

6. (Twice amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 2, wherein said gene encodes a member selected from the group consisting of herpes simplex virus thymidine kinase (HSV-TK), cytosine deaminase, xanthine-guaninephosphoribosyl transferase, purine nucleoside phosphorylase, cytochrome P450 2B1.

7. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 2, wherein said gene is homologous.

8. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 2, wherein said gene encodes a member selected from the group consisting of proto-oncogenes, cytokines, immune stimulatory proteins and anti-angiogenic proteins.

9. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 2, wherein said gene is a member selected from the group consisting of IL-2, IL-12, IL-15 and GM-CSF.

10. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 2, wherein a therapeutically effective amount of said gene is generated at said tumor ~~neoplasia~~.

11. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 1, wherein said ~~nucleic acid-lipid particle comprises~~ cationic lipid is a protonatable lipid having a pKa in the range of about 4 to about 11.

12. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 11, wherein said protonatable lipid is a member selected from the group consisting of DODAC, DODAP, DODMA, DOTAP, DOTMA, DC-Chol, DMRIE, DSDAC and mixtures thereof.

13. (Canceled)

14. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 1 ~~13~~, wherein said lipid conjugate is a member selected from the group consisting of PEG-lipids and PAO-lipids.

15. (As filed) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 13, wherein said lipid conjugate is reversibly associated with an outer lipid monolayer, and

wherein said lipid conjugate exchanges out of said outer lipid monolayer at a rate faster than PEG-CerC20.

16. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 1, wherein said nucleic acid-lipid particle is substantially devoid of detergents and organic solvents.

17. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 1, wherein a therapeutically effective amount of said nucleic acid-lipid particle accumulates at said tumor ~~neoplasia~~.

18. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 1, wherein a therapeutic effect is detected at the site of said tumor ~~neoplasia~~.

19. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 17, wherein said therapeutically effective amount comprises greater than about 0.5% of an administered dose.

20. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 1, wherein said nucleic acid-lipid particle has a diameter of about 50 nm to about 200 nm.

21. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 20, wherein said nucleic acid-lipid particle has a diameter of about 60 nm to about 130 nm.

22. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 20, wherein said nucleic acid-lipid particles are of a uniform size.

23. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 1, wherein said nucleic acid-lipid particle has a nucleic acid to lipid ratio of greater than about 3 mg nucleic acid to mmole of lipid.

24. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 23, wherein said particle has a nucleic acid to lipid ratio of greater than about 14 mg nucleic acid to mmole of lipid.

25. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 23, wherein said particle has a nucleic acid to lipid ratio of greater than about 25 mg nucleic acid to mmole of lipid.

26. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 1, wherein said nucleic acid remains at least 90% intact when said particle containing about 1 μg DNA is treated with about 100 U DNAse 1 in digestion buffer at 37°C for 30 min.

28. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 1, wherein said administering is performed at least once per eight weeks.

35. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal, in accordance with claim 5, wherein said gene encodes a suicide enzyme and said method further comprises administering a prodrug.

36. (Canceled)

37. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 36, wherein said prodrug is administered after the serum-stable nucleic acid-lipid particle.

38. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 36, wherein said prodrug is administered before the serum-stable nucleic acid-lipid particle.

39. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 9, further comprising administering a chemotherapeutic agent.

40. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 39, wherein the chemotherapeutic agent is administered after the serum-stable nucleic acid-lipid particle.

41. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim 39, wherein the chemotherapeutic agent is administered before the serum-stable nucleic acid-lipid particle.

42. (Canceled)

43. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim ~~42~~ 1, wherein the cationic lipid is DODAC.

44. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim ~~42~~ 1, wherein the neutral lipid is DOPE.

45. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim ~~42~~ 1, wherein the lipid portion further comprises a PEG-lipid.

46. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal in accordance with claim ~~42~~ 1, wherein the lipid portion further comprises cholesterol.

47. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal, said method comprising delivering to said tumor ~~administering to said mammal~~ a serum-stable nucleic acid-lipid particle comprising a nucleic acid portion that is fully encapsulated within the lipid portion,

wherein said delivering ~~administration~~ is by injection at an injection site that is distal to said tumor ~~neoplasia~~ in said mammal; and

wherein said tumor ~~neoplasia~~ is responsive to the gene product of the nucleic acid; and

wherein said nucleic-acid lipid particle comprises a cationic lipid, a neutral lipid, and a lipid conjugate that prevents aggregation during formulation.

48. (Once amended) A method of treating a tumor ~~neoplasia~~ in a mammal, said method comprising delivering to said tumor ~~administering to said mammal~~ a serum-stable nucleic acid-lipid particle comprising a nucleic acid portion that is fully encapsulated within the lipid portion,

wherein said delivering ~~administration~~ is by injection at an injection site that is distal to said tumor ~~neoplasia~~ in said mammal; ~~and~~

wherein cells of said tumor ~~neoplasia~~ are transfectable by said nucleic acid-lipid particle; and

and wherein said lipid portion of said nucleic-acid lipid particle comprises a cationic lipid, a neutral lipid, and a lipid conjugate that prevents aggregation during formulation.

49. (As filed) The method of claim 47, wherein said nucleic acid encodes a member selected from the group consisting of: suicide enzymes, toxins, tumor suppressor genes, and cytokines.

50. (Once amended) The method of claim 47, wherein said nucleic acid encodes a suicide enzyme; and said method further comprises administering a prodrug.

51. (As filed) The method of claim 47, wherein said nucleic acid encodes a toxin.

52. (As filed) The method of claim 47, wherein said nucleic acid encodes a tumor suppressor protein.

53. (As filed) The method of claim 47, wherein said nucleic acid encodes a cytokine.

54. (As filed) The method of claim 50, wherein the suicide enzyme is a member selected from the group consisting of: HSV-TK, purine nucleoside phosphorylase, and cytosine deaminase.

55. (Once amended) The method of claim 50, wherein the tumor ~~neoplasia~~ is a melanoma.

56. (Once amended) The method of claim 50, wherein the tumor ~~neoplasia~~ is a colorectal tumor ~~cancer~~.

57. (Once amended) The method of claim 50, wherein the tumor ~~neoplasia~~ is a sarcoma.

58. (As filed) The method of claim 51, wherein the toxin is Pseudomonas exotoxin.

59. (As filed) The method of claim 51, wherein the tumor suppressor protein is apoptin.

60. (As filed) The method of claim ~~51~~ 53, wherein the cytokine is IL-12.

61. (Once amended) The method of claim 51, wherein delivery ~~administration~~ of the serum-stable nucleic acid-lipid particle is intravenous.